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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/716,732	GHOSH ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,22 and 26-30* is/are rejected.

7)☐ Claim(s) *23-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's supplemental response to the Office Action mailed 31 July 2001 is acknowledged (Paper #13 filed 7/3/03). In Amendment-D filed therein claims 1 through 20 were cancelled without prejudice or disclaimer. New claims 21-32 were added. Currently claims 21-32 are pending and under consideration. Objections and Rejections of record set forth in paper #6, which are not presented below have been withdrawn. The rejections over claims 1 and 18 are MOOT because the claims have been canceled.

NEW GROUNDS OF REJECTION NECESSITAED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 21 is indefinite because it is not clear as to how the method will be correlated to neutrite outgrowth. As recited the claim merely requires nuclear imaging along with neutrite imaging to measure a neutrite feature. There is no step of determining or correlating the measured features to neurite outgrowth. Please add the correlation step.

B. Claim 21 is vague and indefinite because it is not clear as to how the nuclear image and the neurite image will be employed to measure neurite outgrowth. The claims merely requires two separate imaging of the nucleus and neurite but does not identify how the images will be related to each other or will measure neurite outgrowth. Please identify the relationship between the two images.

C. Claim 21 is vague and indefinite in utilizing the term "possess" because it is unclear as to what the term encompasses. Is it applicant's intent to imply that the cells will bind a luminescent label, the cells naturally contain a luminescent label, or are synthetically altered to contain a luminescent label. If the cells bind a label it is suggested that the claim clearly recite "binding". Please clarify.

D. Claim 21 step d) recites the limitation "the cell bodies from the neurite image" in step b). However claim 21 step b) does not include "cell bodies". There is insufficient antecedent basis for this limitation in the claim. Step d) should read "a cell body" in order to obviate the rejection.

E. In claim 22 the use of "cell bodies" is not clear because it is not clear if applicant intends to mean the cell bodies in claim 21 step c) or claim 21 step d). Appropriate correction is required.

F. The term "kernel, conditional, and set of nodes" in claims 22 and 24 are relative terms which renders the claim indefinite. The terms "conditional and set of nodes" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Please remove from claim language.

G. Claims 25 and 29 are vague and indefinite because it is not clear what Applicant means regarding the steps being conducted at "multiple time points". As recited the metes and bounds of the claim cannot be determined. It appears that the claims would read on any process wherein each of the steps are conducted sequentially. However does Applicant intend to mean the same step is conducted multiple times. Please clarify.

H. Claims 26 and 27 recite the limitation "neurons " claim 21. However claim 21 does not include "neurons". There is insufficient antecedent basis for this limitation in the claim. Claim 21 should read on "neurons or neuronal cells" in order to obviate the rejection.

I. In claim 28 the use of "cell bodies" is not clear because it is not clear if applicant intends to mean the cell bodies in claim 21 step c) or claim 21 step d). Appropriate correction is required.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 21, 26-27, 29, and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (Cytometry 25:71-81, 1996) in view of McFarlane et al. (Clinicical and Experimental Pharmacology and Physiology, 1995, 22, 362-363) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only).

Dow et al. teach automatic multiparameter fluorescence imaging. Thin tissue sections were stained with Hoechst and three different fluorescent antibodies to antigens that allowed for typing and evaluation of T-cells. This procedure provided the spatial relationships (location) of multiple cell types simultaneously within the tissue. See abstract. The procedure provided an array of locations comprising cells. See figure see for example.

In order to measure the expression of multiple antigens in the sample a first image of the DNA (nuclear material) was employed to identify each nucleated cell and its nuclear boundary. (Applicants nuclear image). In the second step the antibody bound antigen image was used to measure deformable splines in each antigen image. See page 72 1st column. The deformable splines initially positioned at the Hoeschst-stained nuclei or nuclear boundaries (cell bodies) are applied to images of the fluorescently labeled cell surface antigen cell boundary (cell bodies). From the measurements acquired at this boundary (cell bodies) each cell is classified according to antigen expression. See abstract, page 75, and page 76.

This analyses was employed to study cell infiltrate in melanoma tissue sections pre and post treatment (at multiple time points). In this way activated and quiescent cytotoxic and helper T-cells were identified simultaneously in single sections. Page 79 2nd column last paragraph.

Although Dow et al. are silent with respect to the label being a luminescent label it is noted that the type of label employed is deemed mere optimization of the method taught by Dow et al. Absent evidence to the contrary the use of a luminescent label is an obvious design choice routinely modified in the art. This view is supported by the abstract of Wang et al. wherein luminescence labels and fluorescence labels are taught to be interchangeable.

Dow et al. differ from the instant invention in not specifically teaching the detection of neurite outgrowth.

However, McFarland et al. disclose that neurite outgrowth can be assessed by image analysis. See abstract. Specifically changes in neurofilament subunit protein (NF) levels correlated with changes in neurite outgrowth. See page 362 1st column last paragraph.

SKNSH neuroblastoma (neuron cells) was measured by image analysis. The total amount of neuritis was estimated for each of the areas and was expressed as length in mm/mm2 area (neutrite length). The study found that the NF subunit proteins and the neurite length were biphasic and a correlation exists between actual neurite growth and NF protein subunit levels. See page 363 1st column 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure neurite outgrowth as taught by McFarland et al. in the method of Dow et al. because McFarland et al. taught that neurite outgrowth imaging was related to antigen expression (such as NF protein subunits) and the NF proteins are associated with various neuropathology's including human ageing and Alzheimer's disease. Page 362 2nd column. Therefore one would be motivated to measure neurite outgrowth images as an expression of the NF antigen in order to evaluate known neurological disorders. Page 363 2nd column.

II. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (Cytometry 25:71-81, 1996) in view of McFarlane et al. (Clinicical and Experimental Pharmacology and Physiology, 1995, 22, 362-363) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only) and in further view of Ranefall et al. (Analytical Cellular Pathology, 15, 1997, 145-156).

Please see Dow et al. (Cytometry 25:71-81, 1996) in view of McFarlane et al. (Clinicical and Experimental Pharmacology and Physiology, 1995, 22, 362-363) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only) as set forth above.

Dow et al. (Cytometry 25:71-81, 1996) in view of McFarlane et al. (Clinicical and Experimental Pharmacology and Physiology, 1995, 22, 362-363) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only) differ from the instant invention in not specifically teaching nuclear imaging including dilations of the kernel (central or initial nuclear image for further identification.

Ranefall et al. disclose that segmented images (dilations of the kernel image) of stained nuclei can distinguish positive staining reaction from other cell nuclei. See abstract. The full nuclear image is split and spread to more clearly identify the stained cells. See page 146.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure segmented images (dilations of the kernel image) of stained nuclei as taught by Ranefall et al. in the method of Dow et al. in view of McFarlane et al. as supported by Wang et al. because Ranefall et al. taught that this procedure improved reproducibility and more accurately identified positive nuclei. Page 155 Discussion.

III. Claims 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dow et al. (Cytometry 25:71-81, 1996) in view of McFarlane et al.(Clinicical and Experimental Pharmacology and Physiology, 1995, 22, 362-363) as supported by Wang et al. (Pure and Applied Chemistry, 2001, 73(10), 1599-1611 Abstract Only) and in further view of Sano (Current Trends in Neurochemistry, 1997, Vol.1, pages 27-40 Abstract Only).

Please see Dow et al. in view of McFarlane et al. as supported by Wang et al. as set forth above.

Dow et al. in view of McFarlane et al. as supported by Wang et al. differ from the instant invention in not specifically teaching the contacting of the cells with a control compound to stimulate neurite outgrowth and further analyze a tests compounds ability to inhibit neurite outgrowth.

However, Sano disclose this limitation. Specifically, Sano teach the utility of PC12 cells which are NFG-dependent for neurite outgrowth. A MEK inhibitor - PD-98059, inhibited the neurite outgrowth. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure neurite outgrowth with a control compound to stimulate said outgrowth and further analyze a test compound for inhibition as taught by Sano in the method of Dow et al. in view of McFarlane et al. as supported by Wang et al. because Sano taught that this procedure provided predictable neurite outgrowth that allowed for discrimination of inhibitor pathways. See abstract.

Allowable Subject Matter

4. Claims 23-25 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

5. For reasons aforementioned, no claims are allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 271-1600.

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3/17/04

LONG V. LE
SUPERVISORY PATENT EXAMINER
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03/18/04